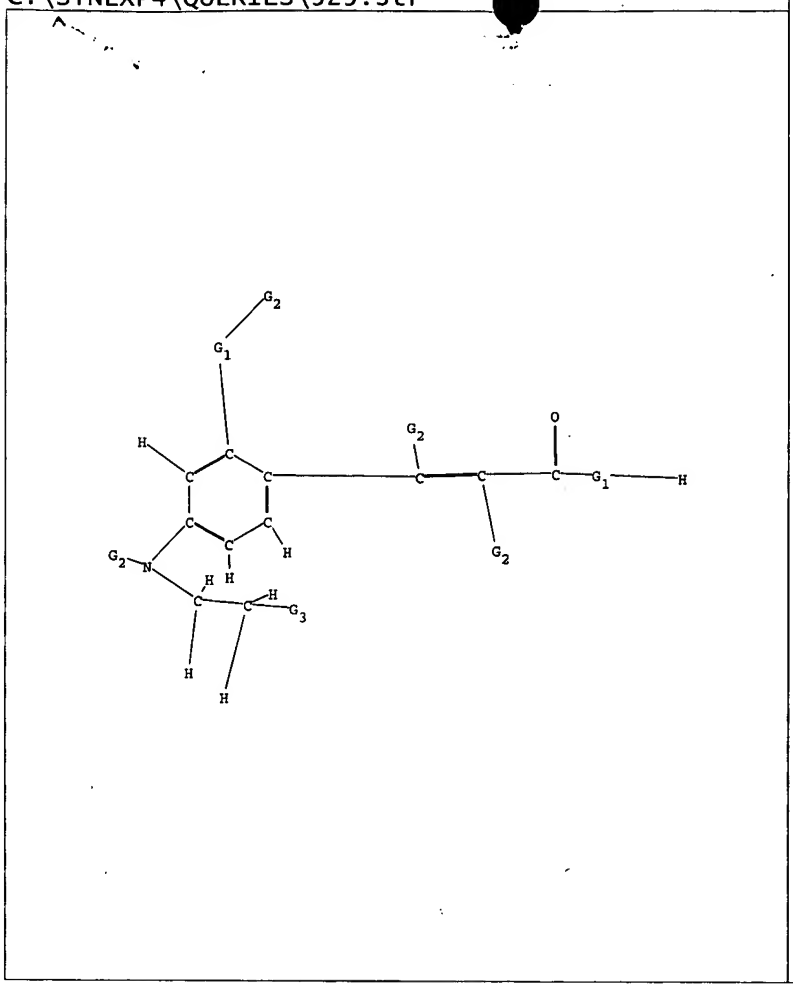
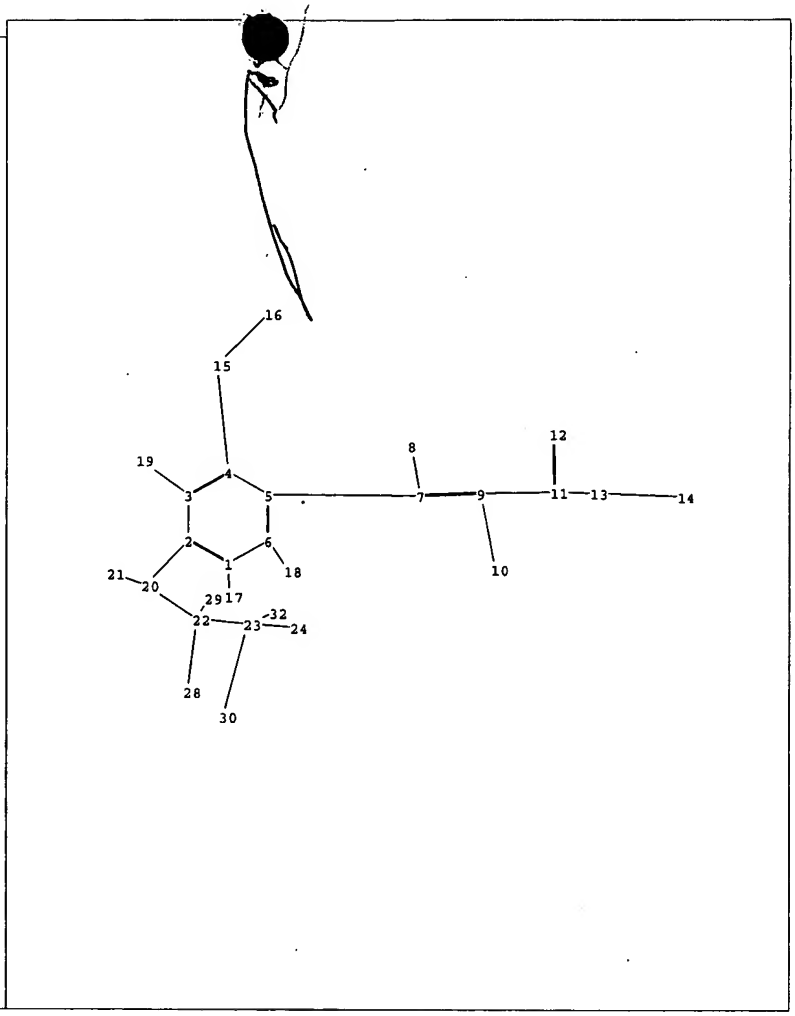
C:\STNEXP4\QUERIES\323.str





chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 28 29 30 32
ring nodes :
1 2 3 4 5 6
chain bonds :
1-17 2-20 3-19 4-15 5-7 6-18 7-8 7-9 9-10 9-11 11-12 11-13 13-14 15-16 20-21
20-22 22-23 22-28 22-29 23-24 23-30 23-32
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
2-20 4-15 7-8 9-10 11-12 11-13 13-14 15-16 20-21 20-22 23-24
exact bonds :
1-17 3-19 5-7 6-18 7-9 9-11 22-23 22-28 22-29 23-30 23-32
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:O,NH,S

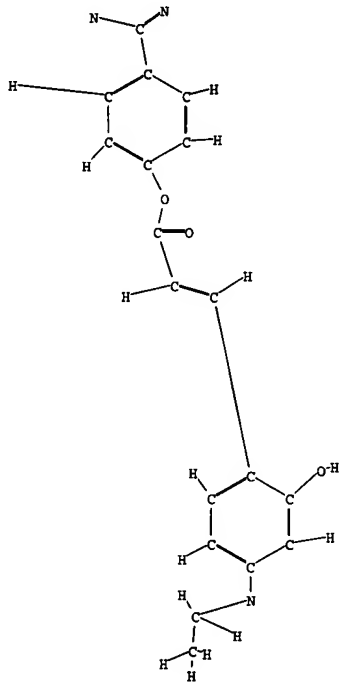
G2:H,CH3

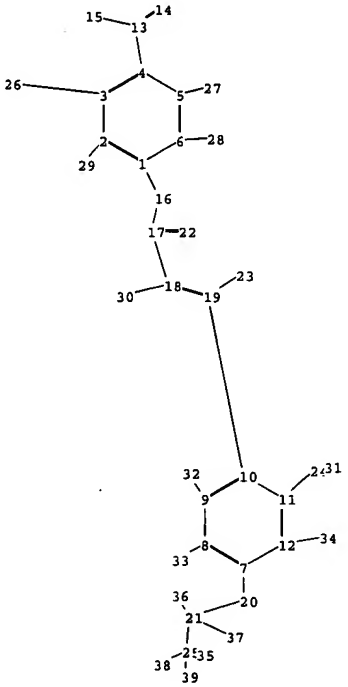
G3:OH,SH

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 28:CLASS 29:CLASS 30:CLASS 32:CLASS

```
=>
Uploading 323.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
   REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




SAMPLE SEARCH INITIATED 15:51:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      2 TO ITERATE

100.0% PROCESSED       2 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            2 TO      124
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1



L3           0 L2

=> s l1  full
   REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




FULL SEARCH INITIATED 15:51:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     36 TO ITERATE

100.0% PROCESSED      36 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L4             0 SEA SSS FUL L1



L5           0 L4

=>
```

C:\STNEXP4\QUERIES\6323.str





chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35
36 37 38 39
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-16 2-29 3-26 4-13 5-27 6-28 7-20 8-33 9-32 10-19 11-24 12-34 13-14 13-15
16-17 17-18 17-22 18-19 18-30 19-23 20-21 21-25 21-36 21-37 24-31 25-35 25-38
25-39
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-16 7-20 11-24 13-14 13-15 16-17 17-22 20-21
exact bonds :
2-29 3-26 4-13 5-27 6-28 8-33 9-32 10-19 12-34 17-18 18-19 18-30 19-23 21-25
21-36 21-37 24-31 25-35 25-38 25-39
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS
39:CLASS

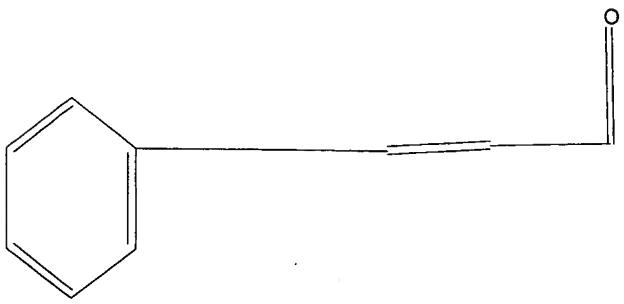
```
=>
Uploading 6323.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
   REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




SAMPLE SEARCH INITIATED 10:35:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1



L3           0 L2

=> s l1 full
   REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




FULL SEARCH INITIATED 10:35:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      2 TO ITERATE

100.0% PROCESSED       2 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L4            0 SEA SSS FUL L1



L5           0 L4

=>
Uploading 6323.str

L6      STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
```

```
L6              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l6
   REGIstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




SAMPLE SEARCH INITIATED 10:38:01 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L7             0 SEA SSS SAM L6



L8           0 L7

=> s l6 full
   REGIstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




FULL SEARCH INITIATED 10:38:07 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      8 TO ITERATE

100.0% PROCESSED       8 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L9             0 SEA SSS FUL L6



L10          0 L9
```

=>
Uploading 323a.str

L6 STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6 STR



G1 O,NH,S

G2 H,Me

G3 OH,SH

Structure attributes must be viewed using STN Express query preparation.

=> s l6
REGIstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 16:35:28 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 14462 TO ITERATE

6.9% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 282042 TO 296438
PROJECTED ANSWERS: 234650 TO 247802

L7 50 SEA SSS SAM L6

L8 15 L7

=> s l6 full
REGIstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 16:35:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 287472 TO ITERATE

100.0% PROCESSED 287472 ITERATIONS 237383 ANSWERS
SEARCH TIME: 00.00.03

L9 237383 SEA SSS FUL L6

L10 103360 L9

=> d l10 and amino and alkoxy
'AND' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'
'AMINO' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'
'AND' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'
'ALKOXY' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,
e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

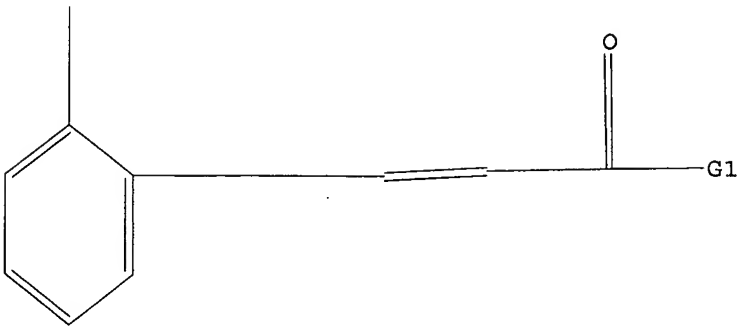
To display a particular field or fields, enter the display field
codes. For a list of the display field codes, enter HELP DFIELDS at
an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO. You may specify the format fields in any order and the
information will be displayed in the same order as the format

specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

=> s l10 and amino and alkoxy
        959512 AMINO
        103121 ALKOXY
L11   1403 L10 AND AMINO AND ALKOXY

d l19
L19 HAS NO ANSWERS
L19 STR



G1 O,NH,S

G2 H,Me

G3 OH,SH

Structure attributes must be viewed using STN Express query preparation.

=> s l19
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 16:51:29 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1549 TO ITERATE

64.6% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 28620 TO 33340
PROJECTED ANSWERS: 13381 TO 16669

L20 50 SEA SSS SAM L19

L21 5 L20

=> d 1-5 ibib abs hitstr

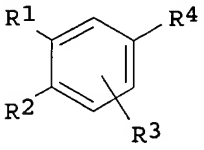
L21 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:454270 CAPLUS
DOCUMENT NUMBER: 139:36341
TITLE: Preparation of cinnamic acids for induction of apoptosis in cancer cells
INVENTOR(S): Dawson, Marcia I.; Fontana, Joseph A.; Zhang, Xiao-Kun; Leid, Mark; Jong, Ling; Hobbs, Peter
PATENT ASSIGNEE(S): The Burnham Institute, USA
SOURCE: PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003048101	A1	20030612	WO 2002-US38506	20021202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003176506	A1	20030918	US 2002-308241	20021202

PRIORITY APPLN. INFO.: US 2001-334081P P 20011130
US 2002-406252P P 20020826

OTHER SOURCE(S): MARPAT 139:36341

GI



I

AB The present invention provides cinnamic acids (shown as I; variables defined below; e.g. (E)-4-[3-(1-Adamantyl)-4-hydroxyphenyl]-3-chlorocinnamic acid (3-Cl-AHPC)) that are inducers or inhibitors of apoptosis or apoptosis preceded by cell-cycle arrest. The present invention provides pharmaceutical compns. and methods for treating mammals with leukemia or other forms of cancer or for treating disease conditions caused by apoptosis of cells. The ability of 3-Cl-AHPC to inhibit the growth of human myeloid leukemia cells was assessed using the human acute megakaryocytic leukemia cell line M07e; exposure of these cells to varying concns. of 3-Cl-AHPC over time resulted in the progressive increase in the inhibition of proliferation; this progressive increase in growth inhibition was accompanied by the onset of apoptosis when 3-Cl-AHPC concns. of 0.5 and 1.0 .mu.M were used; while exposure to 0.2 .mu.M 3-Cl-AHPC resulted in inhibition of growth, no significant increase in apoptosis was noted. In contrast, trans-retinoic acid, a potent activator of the retinoic acid nuclear receptors, did not significantly inhibit M07e proliferation or induce apoptosis in these cells. Results of studies are reported for inhibition of leukemic cell colony formation, inhibition of CFU-GM colony formation, and induction of caspase activity by 3-Cl-AHPC; activation of mitogen-activated protein kinase pathways during 3-Cl-AHPC-mediated apoptosis; 3-Cl-AHPC induction of apoptosis of cancer cells; in vitro efficacy of 3-Cl-AHPC against breast carcinoma cells; in vitro efficacy of 3-Cl-AHPC against primary cultures of human acute myeloid leukemia cells; and 3-Cl-AHPC inhibition of in vivo growth of breast cancer. Although the methods of prepn. are not claimed, 22 example prepns. are included. For I: R1 is C1-10alkyl, C2-10alkenyl, C2-10alkynyl, halo, haloC1-10alkyl, C1-10alkoxy, (C1-10alkyl)mercapto, amino, (C1-10alkyl)NH-, (C1-10alkyl)2N-, C3-8cycloalkyl, C3-8cycloalkenyl, C6-30polycycloalkyl, C6-30polycycloalkenyl, C3-8heterocycloalkyl, C6-30polyheterocycloalkyl, C3-8heterocycloalkenyl, C3-30polyheterocycloalkenyl, aryl, heteroaryl, (C1-10alkyl)C(O)-, (C3-8cycloalkyl)C(O)-, (C3-8cycloalkenyl)C(O)-, (C3-8heterocycloalkyl)C(O)-, or (C3-8heterocycloalkenyl)C(O)-. R2 is H, hydroxy, -SH, amino, -CN, (C1-10alkyl)NH-, (C1-10alkyl)2N-, -COOR14, -C(O)R14, -C(O)N(R14)2, -N(R14)C(O)R14, -P(O)(OR14)2 (phosphonic acid), -S(O)2OR14 (sulfonic acid), -S(O)2N(R14)2 (sulfonamide), -N-C(NH)N(R15)2 (guanidino), (hydroxy)C1-10alkylene-, (C1-10alkyl)C(O)-, -C(O)NHOR14 (hydroxamic acid), or oxime. R3 is H, C1-10alkyl, hydroxy, amino, (C1-10alkyl)NH-, (C1-10alkyl)2N-, -COOR14 (carboxylic acid), -P(O)(OR14)2 (phosphonic acid), -S(O)2OR14 (sulfonic acid), -S(O)2N(R14)2 (sulfonamide),

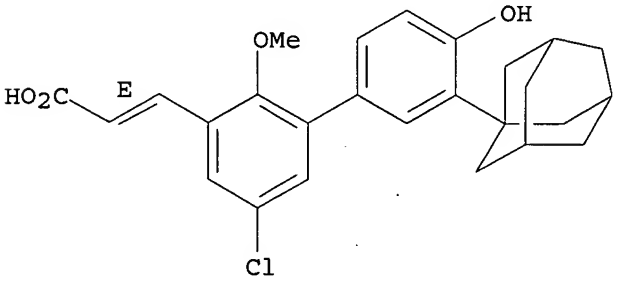
-N-C(NH)N(R15)2 (guanidino), (hydroxy)C1-10alkylene, (C1-10 alkyl)C(O)-, -C(O)NHOR14 (hydroxamic acid), carbonyl oxime, fluoro, chloro, bromo, iodo, -CF3 or nitro; or R1 and R3 taken together with the ring to which they are attached can form a polycyclic group which can be fully satd., partially satd. or arom. R4 is naphthalen-2-yl, quinolin-7-yl, isoquinolin-7-yl, indol-5-yl, indol-2-yl, chroman-6-yl, quinolin-2-yl, isoquinolin-3-yl, Ph (with/without ring atom replacement by S or N), -C(O)R (R = 5-membered hetero ring radical); addnl. details are given in the claims.

IT **540778-97-0P**, (E)-5-[3-(1-Adamantyl)-4-hydroxyphenyl]-3-chloro-6-methoxycinnamic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of cinnamic acids for induction of apoptosis in cancer cells)

RN 540778-97-0 CAPLUS

CN 2-Propenoic acid, 3-(5-chloro-4'-hydroxy-2-methoxy-3'-tricyclo[3.3.1.13,7]dec-1-yl[1,1'-biphenyl]-3-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:278889 CAPLUS

DOCUMENT NUMBER: 139:21996

TITLE: Rational Design, Synthesis, and Structure-Activity Relationships of Novel Factor Xa Inhibitors: (2-Substituted-4-amidinophenyl)pyruvic and -propionic Acids

AUTHOR(S): Sagi, Kazuyuki; Nakagawa, Tadakiyo; Yamanashi, Masahiro; Makino, Shingo; Takahashi, Mitsuo; Takayanagi, Masaru; Takenaka, Kaoru; Suzuki, Nobuyasu; Oono, Seiji; Kataoka, Noriyasu; Ishikawa, Kohki; Shima, Sayaka; Fukuda, Yumiko; Kayahara, Takashi; Takehana, Shunji; Shima, Yoichiro; Tashiro, Kazumi; Yamamoto, Hiroshi; Yoshimoto, Ryota; Iwata, Seinosuke; Tsuji, Takashi; Sakurai, Kuniya; Shoji, Masataka

CORPORATE SOURCE: Pharmaceutical Research Laboratories, Ajinomoto Company Inc., Kawasaki-ku, Kawasaki-shi, 210-8681, Japan

SOURCE: Journal of Medicinal Chemistry (2003), 46(10), 1845-1857
CODEN: JMCMAR; ISSN: 0022-2623

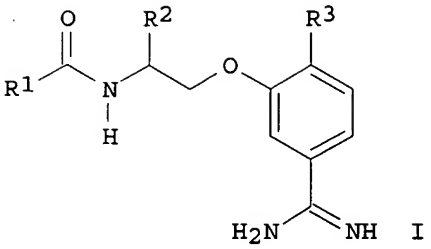
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:21996

GI



I

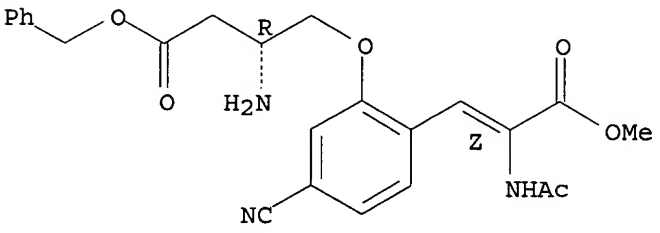
AB An inhibitor of factor Xa (fXa), the m-substituted benzamidine AXC1578 I [R1 = 4-(H2NC:NH)C6H4; R2 = R3 = H; (II)], was structurally modified with the aim of increasing its potency. In particular, pyruvic acid and propionic acid substituents were incorporated into the P1 benzamidine moiety (R3) to introduce a favorable interaction with the oxy-anion hole in the catalytic triad region of fXa. This strategy was based on computational docking studies using the extd. active site of fXa. The validity of the computational model was supported by the acquisition of X-ray crystal structures of the II-trypsin and I [R1 = 4-[4-(1-methylamidinopiperidinyl)oxy]phenyl; R2 = H; R3 = HO2CCOCH2]-trypsin complexes (the homol. around the active sites of fXa and trypsin is high). The above modifications significantly increased the inhibitory activity toward fXa, whereas the high selectivity for fXa vs. thrombin was maintained or enhanced. I [R1 = 4-[4-(1-methylamidinopiperidinyl)oxy]phenyl, 4-[1-(4-pyridyl)]piperidinyl; R2 = H, HO2CCH2; R3 = HO2CCH2CH2, HO2CCOCH2] are considered to be potential lead compds. for the development of orally active anticoagulant drugs because they demonstrated potent activity when administered orally to cynomolgus monkeys.

IT **538335-88-5P 538335-90-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (acylamino)alkoxy benzamidines as factor Xa inhibitors and anticoagulants)

RN 538335-88-5 CAPLUS

CN Butanoic acid, 4-[2-[(1Z)-2-(acetylamino)-3-methoxy-3-oxo-1-propenyl]-5-cyanophenoxy]-3-amino-, phenylmethyl ester, monohydrochloride, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

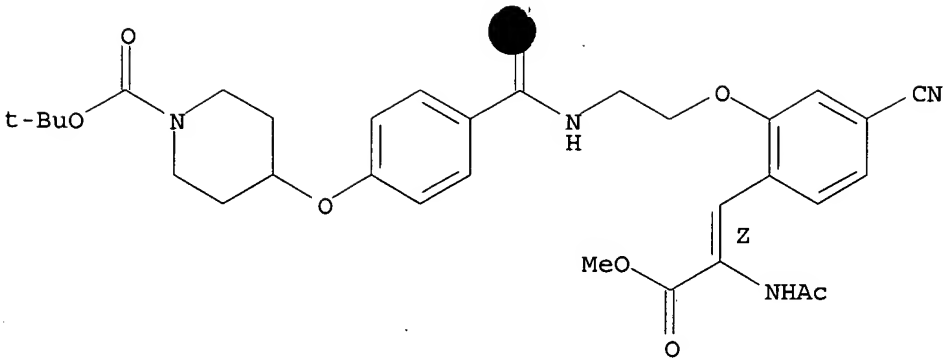


HCl

RN 538335-90-9 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[4-[[[2-[2-[(1Z)-2-(acetylamino)-3-methoxy-3-oxo-1-propenyl]-5-cyanophenoxy]ethyl]amino]carbonyl]phenoxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

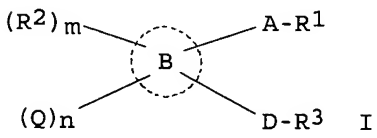
L21 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:154382 CAPLUS
DOCUMENT NUMBER: 138:187795
TITLE: Preparation of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivatives as antagonists of prostaglandin E2 (PEG2) receptors
INVENTOR(S): Tani, Kousuke; Asada, Masaki; Kobayashi, Kaoru; Narita, Masami; Ogawa, Mikio
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 1009 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016254	A1	20030227	WO 2002-JP8120	20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-241867 A 20010809
OTHER SOURCE(S): MARPAT 138:187795
GI



AB Carboxylic acid derivs. (I) and nontoxic salts thereof [wherein R1 = CO2H, CO2R4, CH2OH, COR5SO2R6, CONH2, CH2NR5SO2R6, CH2NR9COR10, CH2NR9CONR5SO2R6, CH2SO2NR9COR10, CH2O2CNR5SO2R6, tetrazole, 1,2,4-oxadiazol-5-one, 1,2,4-oxadiazol-5-thione, 1,2,4-thiadiazol-5-one, etc. (wherein R4 = C1-6 alkyl, hydroxy-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, carboxy-C1-4 alkyl, etc.; R5, R9 = H, C1-6 alkyl; R6 = C1-6 alkyl, C3-15 mono-, di-, or tricarbocyclic, 3- to 13-membered mono-, di-, or tricyclic heterocyclyl, etc.; R10 = H, R6); A = a single bond, C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, etc.; the ring B = C3-12 mono- or dicyclic

carbocyclic ring, 3- to 12-membered mono- or dicyclic heterocyclic ring; R2 = C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C2-6 alkenyl, C2-6 alkynyl, halo, CHF2, CF3, NO2, cyano, Ph, oxo; m, n = 0,1,2; Q = (C1-4 alkylene, C2-4 alkenylene, or C2-4 alkynylene)-Cyc2, -C1-4 alkylene-Z-Cyc3, amino-C1-4 alkyl, cyano-C1-4 alkyl, acylamino-C1-4 alkyl, 3- to 7-membered monocyclic carbocyclyl, 3- to 6-membered monocyclic heterocyclyl, etc. (wherein Cyc2, Cyc3 = C3-15 mono-, di-, or tricyclic carbocyclyl or heterocyclyl, etc.; Z = O, S, SO, SO2, NH, NHCO, etc.); D = an linking chain consisting of 1-2 or 3-6 of atoms selected from C, N, O, or S, etc.; R3 = C1-6 alkyl, C3-15 mono-, di-, or tricyclic carbocyclyl, 3- to 15-membered mono-, di-, or tricyclic heterocyclyl, etc.] are prepd. These carboxylic acid derivs. include phenylpropanoic acid, phenylpropenoic acid, phenylpropanamide, phenylpropenamide, 3-oxoisoindolin-1-ylacetic acid, benzylbenzoic acid, benzylaminoacetic acid, pyrazolylmethylbenzoic acid, benzoylaminoacetic acid, (pyrazolylmethylphenyl)propenoic acid, pyrazolylmethylpropanoic acid, (pyridinyloxyphenyl)propanoic acid, phenoxyacetic acid, phenylbutanoic acid, (pyrazolylmethyl)propanamide, (piperazinylmethylphenyl)propanamide, (morpholinylmethylphenyl)propanamide, (pyridinyloxyphenyl)propanamide, (pyrazolylmethyl)propenamide (oxoimidazolidinylmethylphenyl)propanamide, (oxopyrrolidinylmethylphenyl)propenamide, (thiophenylmethylphenyl)propenamide, (pyrazolylmethylphenylamino)acetamide, (thiazolylaminomethylphenyl)propanamide, thiophenylpropenamide, (pyrazolylmethylphenoxy)acetamide, (phenoxymethyl)benzamide, (pyrazolylmethylphenylethyl)-1,2,4-oxadiazol-5-one, and (pyrazolylmethylphenylindolyl)acetic acid. Because of binding to PEG2 receptors, in particular, subtype EP3 and/or subtype EP4 and having antagonism, the compds. I are useful in preventing and/or treating diseases such as pain, allodynia, hyperalgesia, pruritus (itching), urticaria, atopic dermatitis, contact dermatitis, Urushi (Japanese lacquer tree) dermatitis, allergic conjunctivitis, symptoms during dialysis, asthma, rhinitis, allergic rhinitis, nasal congestion, sneeze, psoriasis, pollakiuria (increased urinary frequency), urination disorder, ejaculation (semination) disorder, fever (pyrexia), systemic inflammation reaction, learning disorder, Alzheimer's disease, neovascularization, cancer formation, cancer proliferation, cancer metastasis to organs, cancer metastasis to bone, hypercalcemia accompanied by cancer metastasis to bone, retinopathy, rubrum, erythema (rash), leucoma, skin moth-patch, heat burn, burn, steroid burn, kidney failure, nephropathy, acute or chronic nephritis, blood electrolyte disorder, imminent abortion, threatened abortion, excessive menstruation, dysmenorrhea, endometriosis, premenstrual syndrome, uterine gland myopathy, reprodn. disorder, and stress. They are also useful in preventing and/or treating anxiety, depression, psychophysiol. disorder, mental retardation, thrombus, embolism, transient ischemic attack, cerebral infarction, atheroma, organ transplant, heart failure, hypertension, myocardial infarction, arteriosclerosis, circulation disorders or ulcers assocd. therewith, nerve disorders, vascular dementia, edema, diarrhea, constipation, biliary excretion disorder, ulcerative colitis, Crohn's disease, irritable bowel syndrome, redn. of rebound after using steroid drugs, aids for decreasing or removing steroid drugs, bone diseases, systemic granuloma, immune diseases, pyorrhea alveolaris, gingivitis, periodontal disease, nerve cell death, lung disorder, liver disorder, acute hepatitis, myocardial ischemia, Kawasaki disease, multiple organ failure, chronic headache, angiitis, venous failure, varicose vein (varicosis), anal fistula, diabetes insipidus, neonatal patent ductus arteriosus, and cholelithiasis. Thus, 4-hydroxymethyl-2-[2-(naphthalen-2-yl)ethoxy]cinnamic acid Et ester was mesylated by methanesulfonyl chloride in the presence of Et3N in THF at 0.degree. for 15 min and condensed with pyrazole in the presence of NaH in DMF at 0.degree. to give 2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid Et ester. 4-[2-[[2-(Naphthalen-1-yl)propanoyl]amino]-4-methylthiomethylphenyl]butanoic acid inhibited the binding of [3H]PGE2 to prostaglandin E2 (PEG2) receptor subtype EP1, Ep2, EP3, and EP4 expressed in CHO cells with Ki of >10, >10, 0.27, and 0.038 .mu.M, resp. A tablet formulation contg. (2E)-2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid was described.

IT **499143-68-9P 499144-08-0P 499151-46-1P**

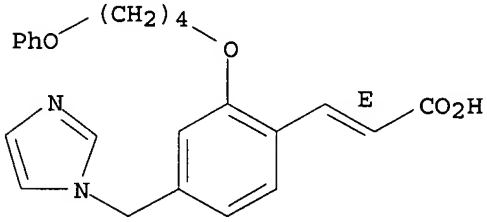
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivs. as antagonists of prostaglandin E2 (PEG2) receptors as therapeutic agents)

RN 499143-68-9 CAPLUS

CN 2-Propenoic acid, 3-[4-(1H-imidazol-1-ylmethyl)-2-(4-phenoxybutoxy)phenyl]-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

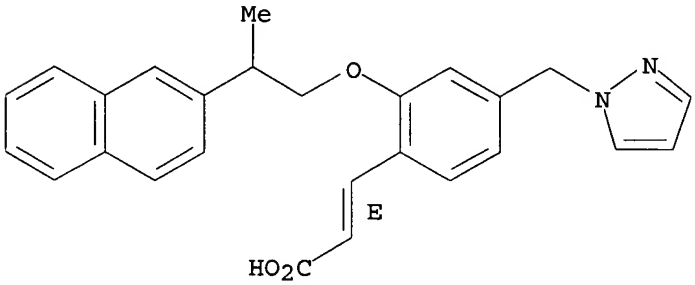


● HCl

RN 499144-08-0 CAPLUS

CN 2-Propenoic acid, 3-[2-[2-(2-naphthalenyl)propoxy]-4-(1H-pyrazol-1-ylmethyl)phenyl]-, (2E)- (9CI) (CA INDEX NAME)

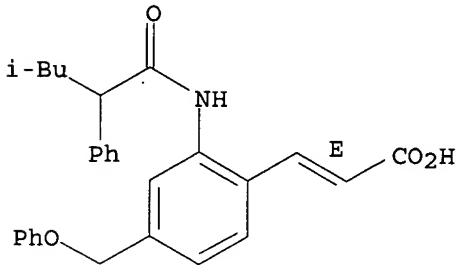
Double bond geometry as shown.



RN 499151-46-1 CAPLUS

CN 2-Propenoic acid, 3-[2-[(4-methyl-1-oxo-2-phenylpentyl)amino]-4-(phenoxymethyl)phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



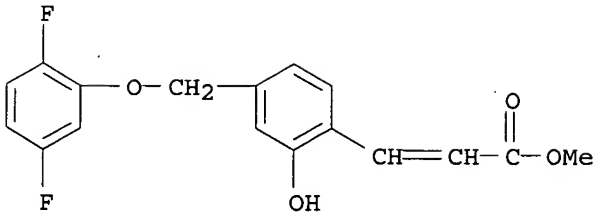
IT **499157-88-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivs. as antagonists of prostaglandin E2 (PEG2) receptors as therapeutic agents)

RN 499157-88-9 CAPLUS

CN 2-Propenoic acid, 3-[4-[(2,5-difluorophenoxy)methyl]-2-hydroxyphenyl]-, methyl ester (9CI) (CA INDEX NAME)



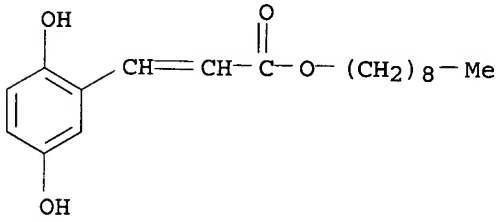
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:940366 CAPLUS
DOCUMENT NUMBER: 138:385123
TITLE: Synthesis and antitumor activity of alkyl 2,5-dihydroxycinnamates
AUTHOR(S): Nguyen, Hai Nam; Ahn, Byung-Zun
CORPORATE SOURCE: College of Pharmacy, Chungnam National University, S. Korea
SOURCE: Tap Chi Hoa Hoc (2002), 40(3), 111-115
CODEN: TCHHDC; ISSN: 0378-2336
PUBLISHER: Toa Soan Tap Chi Hoa Hoc
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:385123

AB A series of alkyl 2,5-dihydroxycinnamates (2a.apprx.i) were synthesized and evaluated for cytotoxicity and antitumor activity. The cytotoxicity decreased with alkyl chains from Me to n-pentyl. However, further prolongation proved to be beneficial for bioactivity with cytotoxicity peaked when alkyl chain being n-nonyl (2i). Two compds. 2a and 2i showed significant antitumor activities in BDF1/B16 model.

IT **528603-13-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of alkyl 2,5-dihydroxycinnamates and antitumor activity thereof)

RN 528603-13-6 CAPLUS
CN 2-Propenoic acid, 3-(2,5-dihydroxyphenyl)-, nonyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

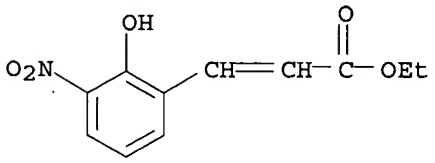
L21 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:835620 CAPLUS
DOCUMENT NUMBER: 139:22119
TITLE: Product class 13: benzoxazoles and other annulated oxazoles
AUTHOR(S): Boyd, G. V.
CORPORATE SOURCE: Givataim, 53460, Israel
SOURCE: Science of Synthesis (2002), 11, 481-492
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review describes the different methods for the synthesis of benzoxazoles and other annulated oxazoles.

IT **538311-22-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of benzoxazoles and annulated oxazoles via ring closing reactions or ring transformation reactions)

RN 538311-22-7 CAPLUS

CN 2-Propenoic acid, 3-(2-hydroxy-3-nitrophenyl)-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 16:55:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 31652 TO ITERATE

100.0% PROCESSED 31652 ITERATIONS 15524 ANSWERS
SEARCH TIME: 00.00.01

L22 15524 SEA SSS FUL L19

L23 4107 L22

=> s l23 and amino and alkoxy
959512 AMINO
103121 ALKOXY
L24 158 L23 AND AMINO AND ALKOXY

=> d 150-158 ibib abs hitstr

L24 ANSWER 150 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:586887 CAPLUS
DOCUMENT NUMBER: 95:186887
TITLE: 2- Or 3-(substituted **amino**)phenyl compounds for use as antiatherosclerotic agents
INVENTOR(S): Shepherd, Robert G.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Def. Publ. U. S. Pat. Off. T, 50 pp.
CODEN: USXXBN
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 100403	H	19810303	US 1979-85650	19791017
GB 2062621	A	19810528	GB 1979-37886	19791101

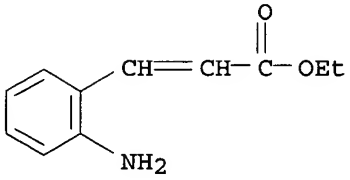
PRIORITY APPLN. INFO.: US 1979-85650 19791017

AB Title compds. RR1NC6H4R2 (I; R = alkyl, alkenyl, cycloalkylalkylene; R1 = H, Me, CO2Me, Ac, succinyl, alkylsulfonate; R2 = optionally substituted CO2H, alkanoyl, OH, **alkoxy**, dialkylaminoalkoxy, PhCH2O, PhO, pyridyloxy, alkylamino, HO3SCH2CH2NH) useful as hypolipidemics or anti-atherosclerotics (no data) were prepd. Thus, 3-H2NC6H4CO2Me was heated at 135.degree. 20 h with Me(CH2)15Br, K2CO3, and (Me2N)3P(O) to give 3-H2NC6H4CO2Me.

IT **79655-96-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of)

RN 79655-96-2 CAPLUS

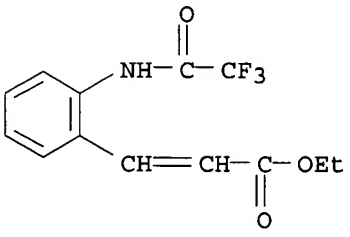
CN 2-Propenoic acid, 3-(2-aminophenyl)-, ethyl ester (9CI) (CA INDEX NAME)



IT **79656-13-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and bromination of)

RN 79656-13-6 CAPLUS

CN 2-Propenoic acid, 3-[2-[(trifluoroacetyl)amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 151 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1980:471786 CAPLUS

DOCUMENT NUMBER: 93:71786

TITLE: 1,2,4-Triazole derivatives

INVENTOR(S): Mildenberger, Hilmar; Maier, Thomas; Sachse, Burkhard

PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

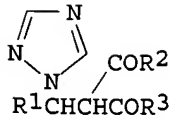
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2836945	A1	19800313	DE 1978-2836945	19780824
ES 483466	A1	19800416	ES 1979-483466	19790817
EP 8458	A1	19800305	EP 1979-103077	19790822
R: AT, BE, CH, DE, FR, GB, IT, NL, SE				
DD 145990	C	19810121	DD 1979-215125	19790822
AU 7950215	A1	19800228	AU 1979-50215	19790823
JP 55031093	A2	19800305	JP 1979-106720	19790823
BR 7905429	A	19800520	BR 1979-5429	19790823
ZA 7904445	A	19800827	ZA 1979-4445	19790823

PRIORITY APPLN. INFO.: DE 1978-2836945 19780824

GI



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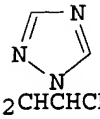


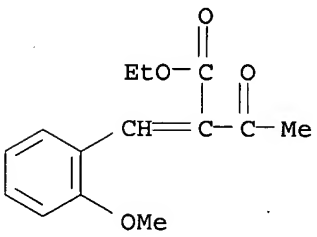
II

AB Triazoles I [R1 = C1-12 alkyl, C5-9 cycloalkyl, cycloalkenyl, Ph [optionally substituted with 1-3 alkyl, halo, C1-5 **alkoxy**, OH, NO2, di(C1-6 alkyl) **amino**, methylenedioxy], furanyl, thienyl, pyridyl; R2, R3 = C1-12 alkyl, C5-9 cycloalkyl, Ph (optionally substituted with 1-3 C1-12 alkyl, halo, C1-5 **alkoxy**, OH), C1-12 **alkoxy**, C5-6 cycloalkoxy, PhCH2O], useful as agricultural fungicides (extensive data tabulated), were prepd. by addn. reaction of 1,2,4-triazole to R1CH:C(COR2)COR3 in the presence of a basic catalyst. Thus, a mixt. of Me2CHCH:C(CO2Me)2, 1,2,4-triazole, and NEt3 reacted exothermally (70.degree.) and after 30 min was stirred 7 h at 90.degree. to give 96.65% malonate II.

IT **15725-24-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(addn. reaction of, with triazole)

RN 15725-24-3 CAPLUS

CN Butanoic acid, 2-[(2-methoxyphenyl)methylene]-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 152 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1978:442891 CAPLUS

DOCUMENT NUMBER: 89:42891

TITLE: Syntheses of nitrophenanthrene-9-carboxylates with various **alkoxy** substituents

AUTHOR(S): Pailer, Matthias; Willvonseder, Gerhard

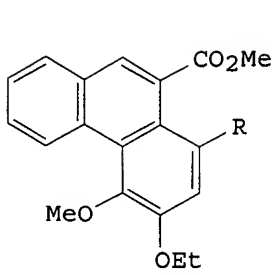
CORPORATE SOURCE: Pharm.-Chem. Inst., Univ. Wien, Vienna, Austria

SOURCE: Monatshefte fuer Chemie (1978), 109(2), 511-21
CODEN: MOCMB7; ISSN: 0026-9247

DOCUMENT TYPE: Journal

LANGUAGE: German

GI



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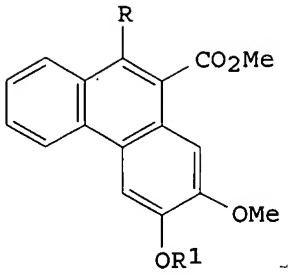
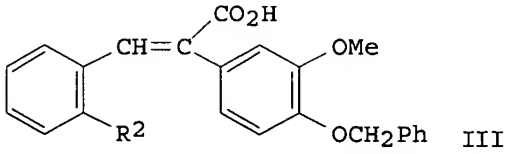


II



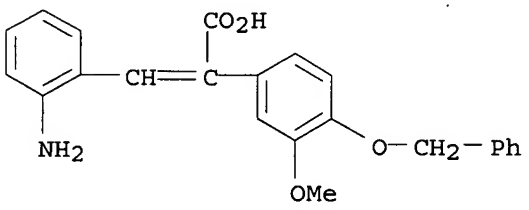
III

AB The nitrophenanthrenecarboxylates I (R = NO2) and II (R = NO2, R1 = Et, Bu, CH2CHMe2, n-hexyl) were prepd. by nitrating I and II (R = H). The key intermediate II (R = R1 = H) was obtained by condensing o-O2NC6H4CHO with 3,4-MeO(PhCH2O)C6H3CO2H, reducing the resulting III (R2 = NO2), cyclizing the **amino** deriv. (III, R2 = NH2), and reducing II (R = H, R1 = CH2Ph).

IT **67064-66-8P 67064-67-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)

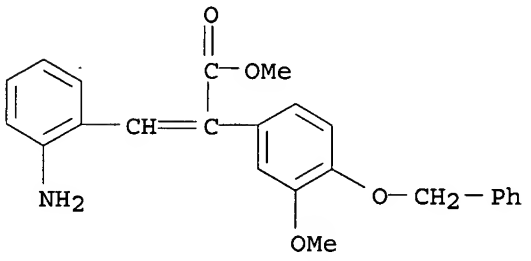
RN 67064-66-8 CAPLUS

CN Benzeneacetic acid, .alpha.-[(2-aminophenyl)methylene]-3-methoxy-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 67064-67-9 CAPLUS

CN Benzeneacetic acid, .alpha.-[(2-aminophenyl)methylene]-3-methoxy-4-(phenylmethoxy)-, methyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 153 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1970:78584 CAPLUS

DOCUMENT NUMBER: 72:78584

TITLE: Chemistry of bis(2-cyanoethyl) derivatives of some aromatic amines. V. Preparation of some new tertiary aminobenzaldehydes and a study of some of their reactions

AUTHOR(S): Jolly, V. S.; Ittyerah, P. I.

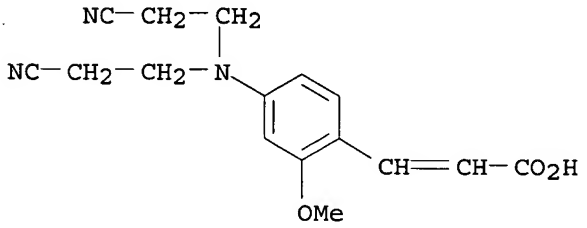
CORPORATE SOURCE: Chem. Lab., St. John's Coll., Agra, India

SOURCE: Journal of the Indian Chemical Society (1969), 46(11), 997-1002
CODEN: JICSAH; ISSN: 0019-4522
DOCUMENT TYPE: Journal
LANGUAGE: English

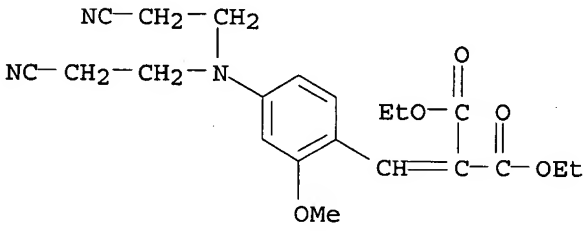
AB 4-[N,N-bis(2-cyanoethyl)**amino**]-2-ethoxy- and 2,6-(dimethylamino)benzaldehydes have been prepd. for the first time. Some of the reactions of these aldehydes and also of 4-[N,N-bis-(2-cyanoethyl)**amino**]-2-methoxy- and 2-methylbenzaldehydes have been studied. p-[N-Methyl-N-(2'-cyanoethyl)**amino**]benzaldehyde which has so farbeen known through some of its derivs. has now been isolated in the pure form.

IT **28006-72-6P 28006-73-7P 28006-75-9P 28006-79-3P 28006-81-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

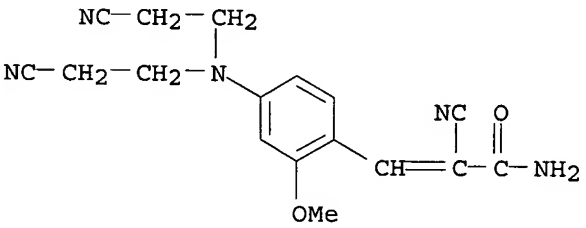
RN 28006-72-6 CAPLUS
CN Cinnamic acid, 4-[bis(2-cyanoethyl)amino]-2-methoxy- (8CI) (CA INDEX NAME)



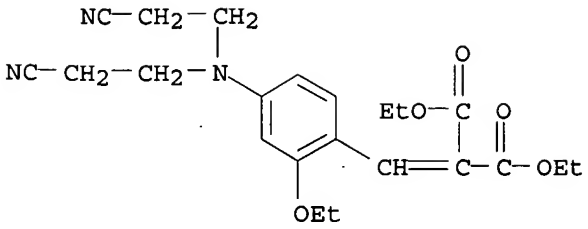
RN 28006-73-7 CAPLUS
CN Malonic acid, [4-[bis(2-cyanoethyl)amino]-2-methoxybenzylidene]-, diethyl ester (8CI) (CA INDEX NAME)



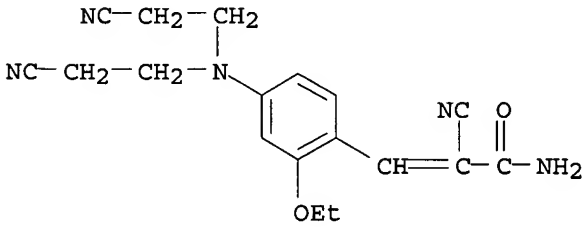
RN 28006-75-9 CAPLUS
CN Cinnamamide, 4-[bis(2-cyanoethyl)amino]-.alpha.-cyano-2-methoxy- (8CI) (CA INDEX NAME)



RN 28006-79-3 CAPLUS
CN Malonic acid, [4-[bis(2-cyanoethyl)amino]-2-ethoxybenzylidene]-, diethyl ester (8CI) (CA INDEX NAME)



RN 28006-81-7 CAPLUS
CN Cinnamamide, 4-[bis(2-cyanoethyl)amino]-.alpha.-cyano-2-ethoxy- (8CI) (CA INDEX NAME)



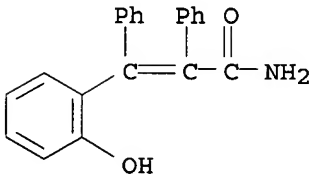
L24 ANSWER 154 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1968:418873 CAPLUS
DOCUMENT NUMBER: 69:18873
TITLE: Ether-linked basic amines of triarylacrylamides
INVENTOR(S): Allen, Robert E.; Ambrus, Laszlo
PATENT ASSIGNEE(S): Cutter Laboratories Inc.
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3361813	A	19680102	US 1964-380086	19640702

PRIORITY APPLN. INFO.: US 1964-380086 19640702
GI For diagram(s), see printed CA Issue.
AB The title compds. were prepd. by reaction of a phenolic hydroxy-contg. triarylacrylamide with an aminoalkyl halide. A soln. of 90 g. p-MeOC6H4CH2CN in 200 ml. dry C6H6 was added to a stirred refluxing suspension of 110 g. Ph2CO (I) and 40 g. NaH (II) (53% suspension in mineral oil), the mixt. refluxed an addnl. 4 hrs., kept at room temp. 16 hrs., excess II decompd. with H2O, and the org. layer sepd. to give 3,3-diphenyl-2-(r-methoxyphenyl)acrylonitrile (III) (R = R1 = H, R2 = p-OMe) (IV), yellow, m. 148-9.degree.. IV (90 g.) and 126 g. C5H5N.HCl was refluxed 30 min., the mixt. cooled, dild. with H2O, and filtered, the crude ppt. dissolved in 1 1. 5% soln. NaOH, the resulting soln. filtered, and the filtrate acidified with 1 1. 5% soln. HCl to give III (R = R1 = H, R2 = p-OH) (V), m. 229-30.degree.. V was also prepd. by the acid decompn. of III (R = R1 = H, R2 = tetrahydropyran-2-yloxy), m. .apprx.143-4.degree. [prepd. by condensation of I with 4-(tetrahydropyran-2-yloxy)phenylacetonitrile, m. 64-6.degree.]. A mixt. of 29.7 g. V and 120 g. NaOH in 400 ml. isoamyl alc. was refluxed 3 hrs., and the mixt. cooled to give a ppt. which was dissolved in 500 ml. warm H2O, and repptd. by diln. with excess 10% soln. HCl to give 3,3-diphenyl1-2-(4-hydroxyphenyl)acrylamide (VI) (R = R1 = H, R2 = p-OH), m. 284-5.degree.. A mixt. of 100 g. p-HOC6H4COPh and 50 g. dihydropyran was dissolved in 500 ml. warm dry C6H6 and 2 ml. concd. HCl and the mixt. refluxed 4 hrs. and kept 16 hrs. at room temp. to give 4-(tetrahydropyran-2-yloxy)benzophenone (VII), m. 49-51.degree. (pentane). To a refluxing suspension of 8 g. II in 200 ml. Et2O a soln. of 11.4 g. PhCH2CN in 200 ml. Et2O was added during 2 hrs. and the mixt. refluxed an addnl. hr., treated with a soln.

of 28 g. VII in 100 ml. Et[redacted], refluxed 2 hrs., and kept 16 [redacted]s. at room temp. to give III (R = R2 = H, R1 = 4-tetrahydropyran-2-yloxy) (VIII), m. 118-44.degree.. A soln. of VIII in 100 ml. hot HOAc contg. a few drops concd. H2SO4 dild. with H2O gave III (R = R2 = H, R1 = p-OH), yellow, m. 207-8.degree.. Other III prepd. were (R, R1, R2, and m.p. given): p-Me, p-Me, p-OMe, 146-8.degree. (iso-PrOH); p-Me, p-Me, p-OH, 229-30.degree.; p-MeO, p-MeO, p-OH, 217-19.degree.; p-Cl, p-Cl, p-OH, 252-4.degree. (HOAc); p-OH, H, p-MeO, 189-91.degree. (HOAc); p-Q (Q = tetrahydropyran-2-yloxy), H, p-Cl, 183-4.degree. (EtOH); p-OH, H, p-Cl, 175-7.degree. and 187-9.degree. (geometric isomers); p-NMe2, p-NMe2, p-Q, 189-91.degree.; p-NMe2, p-NMe2, p-OH, 240-2.degree.; H, p-Q, p-Q, 189-91.degree.; p-OH, H, p-OH, 261-2.degree. and 263-4.degree. (geometric isomers); H, p-OH, H, -; p-CF3, p-CF3, p-MeO, -; p-CF3, p-CF3, p-OH, -. Other VI prepd. were (R, R1, and R2 given): p-Me, p-Me, p-OH, m. 254-5.degree.; p-MeO, p-MeO, p-OH; p-Cl, p-Cl, p-OH; H, p-OH, H; p-OH, H, p-MeO; p-OH, H, p-Cl; p-NMe2, p-NMe2, p-Q, m. 189-91.degree. (HCONMe2-EtOH); p-NMe2, p-NMe2, p-OH; p-OH, H, p-OH; H, p-OH, H; p-CF3, p-CF3, p-OH. Also prepd. were the HCl salts of the following VI (R, R1, and R2 given): H, H, p-O (CH2)2NEt2, m. 104.degree. (iso-PrOH); p-Me, p-Me, p-O (CH2)2NEt2, m. 177-8.degree.; p-Cl, p-Cl, p-O (CH2)2NEt2; p-OH, p-OH, p-O (CH2)2NEt2; H, H, p-O (CH2)2NMe2; H, H, p-O (CH2)3NMe2; p-O (CH2)2NEt2, H, H; p-O (CH2)2NEt2, H, p-MeO; p-O (CH2)2NEt2, H, p-Cl; p-NMe2, p-NMe2, p-O (CH2)2NEt2; p-O (CH2)2NEt2, H, p-O (CH2)2NEt2; o-O (CH2)2NEt2, H, H; p-CF3, p-CF3, p-O (CH2)2NEts. Also prepd. were 3,3-diphenyl-2-[4-(2-piperidinoethoxy)phenyl]acrylamide-HCl and the corresponding 2-(1-pyrrolidinyl)ethoxy analog. A soln. of VI (R = R1 = H, R2 = O(CH2)2NEt2) (0.028 mole) in 300 ml. MeOH treated with 10 ml. 30% H2O2 was kept 20 hrs. at room temp., the solvent removed in vacuo, and the residual oil taken up in 100 ml. EtOAc and acidified to .apprx.pH 2 with alc. HCl soln. to give 2-[4-(2-diethylaminoethoxy)phenyl]-3,3-diphenylacrylamide N-oxide, HCl salt, melted with decompn. The N-oxide base was obtained by working up the product of the H2O2 reaction, and sepg. it without prior acidification. These compds. are characterized by gonadotrophic-inhibitory, and uterotrophic activity, herbicidal, and insecticidal activity. Some compds. exhibit antilipase or lipase inhibitory activity.

IT **19094-22-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 19094-22-5 CAPLUS
CN Acrylamide, 3-(o-hydroxyphenyl)-2,3-diphenyl- (8CI) (CA INDEX NAME)



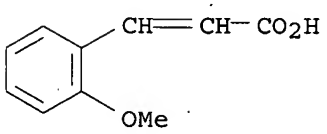
L24 ANSWER 155 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1959:11539 CAPLUS
DOCUMENT NUMBER: 53:11539
ORIGINAL REFERENCE NO.: 53:2106b-e
TITLE: Synthesis of .beta.-**amino** acids from aromatic hydroxy and **alkoxy** aldehydes
AUTHOR(S): Rodionov, V. M.; Dudinskaya, A. A.; Avramenko, V. G.; Suvorov, N. N.
CORPORATE SOURCE: S. Ordzhonikidze All-Union Chem. Pharm. Sci. Research Inst., Moscow
SOURCE: Zhurnal Obshchei Khimii (1958), 28, 2242-6
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 21, 1257. The present study examd. some exceptions from the usual course of the Rodionov reaction for synthesis of **amino** acids. Refluxing 5 g. salicylaldehyde, 4.8 g. CH2(CO2H)2, 7.5 g. NH4OAc,

and 10 ml. EtOH 3 hrs. gave coumarin-3-carboxylic acid, m. [redacted]5-7.degree.. Reaction of m-HOC6H4CHO with CH2(CO2H)2 and NH4OAc in BuOH in 2.5 hrs. gave 52.6% .beta.-(3-hydroxyphenyl)-.beta.-alanine, decomp. 222-3.degree.. p-HOC6H4CHO in a similar reaction in 3 hrs. gave di-NH4 4-hydroxybenzylidenemalonate (I), decomp. 188-90.degree., which heated with NaOH and acidified gave the free acid, decomp. 174-5.degree., which refluxed with H2O 2.5 hrs. lost CO2 and gave p-coumaric acid, m. 194-5.degree.. The mother liquor after isolation of I gave 25.5% .beta.-(p-hydroxyphenyl)-.beta.-alanine, decomp. 173-4.5.degree., whose dibenzoyl deriv. decomp. 194-4.5.degree.. Similarly .omicron.-MeOC6H4CHO, CH2(CO2H)2, and NH4OAc in EtOH in 5 hrs. gave only 2-methoxycinnamic acid, m. 183-4.degree.. The same reaction with the m-methoxy isomer gave 62.2% .beta.-(m-methoxyphenyl)-.beta.-alanine, decomp. 216.degree.. Similarly p-MeOC6H4CHO gave 56% .beta.-(p-methoxyphenyl)-.beta.-alanine, decomp. 228.degree.. 3,4-Dihydroxybenzaldehyde treated similarly gave only 3,4-dihydroxycinnamic acid, m. 194-5.degree.. Vanillin in this reaction gave 40% di-NH4 3-methoxy-4-hydroxybenzylidenemalonate, decomp. 193-3.5.degree., which gave the free acid, decomp. 212.degree., which with Ac2O gave the acetyl deriv., decomp. 173.degree.. 3,4-Dimethoxybenzaldehyde similarly treated gave 52% .beta.-(3,4-dimethoxyphenyl)-.beta.-alanine, decomp. 221.5-2.degree., and some 3,4-dimethoxycinnamic acid, m. 180-1.degree.. The former with Ac2O in aq. KOH gave N-acetyl-.beta.-(3,4-dimethoxyphenyl)-.beta.-alanine, m. 169-70.degree..

IT **6099-03-2**, Cinnamic acid, o-methoxy-
(formation in reaction of NH4OAc, o-anisaldehyde and malonic acid)

RN 6099-03-2 CAPLUS

CN 2-Propenoic acid, 3-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



L24 ANSWER 156 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1957:74459 CAPLUS

DOCUMENT NUMBER: 51:74459

ORIGINAL REFERENCE NO.: 51:13409g-i,13410a-b

TITLE: Methine dyes for synthetic fibers

INVENTOR(S): Kartinos, Nicholas J.; Normington, James B.; Williams, Wm. W.

PATENT ASSIGNEE(S): General Aniline & Film Corp.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2789125		19570416	US	

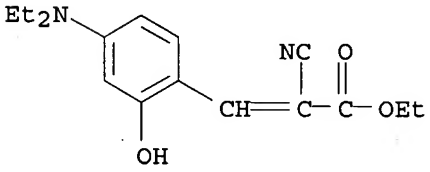
AB Products, having high tinctorial strength, excellent light-, chlorine-, and wash-fastness, good sublimation and fluorescent properties, and adaptability as fluorescent pigments and brightening agents, particularly for synthetic fibers, such as acetate rayons, are obtained by condensing a 2-substituted 4-[dialkyl- or bis(alkylcarboxyalkyl)**amino**]benzaldehyde with an alkyl cyanoacetate or cyanoethyl cyanoacetate in the presence of a basic or acid condensing agent. The dyes have the formula 2,4-R'(R2N)C6H3CH:C(CN)CO2CH2CH2CN, where R is a lower alkyl group, and R' is a halogen, hydroxy, or lower **alkoxy** group.
2-Ethoxy-4-diethylaminobenzaldehyde (I), m. 45.8.degree., was obtained in 38% yield by combining 96.5 g. of N,N-diethyl-m-phenetidine and 73 g. of dimethylformamide, cooling to 10.degree., adding 92 ml. of POCl3 dropwise during 45 min., warming on a steam bath for 4 hrs., cooling, drowning in ice water, and adding 300 ml. of 40% NaOH soln. until the pH was 3-5. By mixing 11.05 g. of I, 6.8 g. of Et cyanoacetate (II), 30 ml. of iso-PrOH (III), and 5 drops of piperidine (IV), mildly refluxing for 1 hr.,

collecting and drying the light-orange solid gave Et .alpha.-cyano-4-(diethylamino)-2-ethoxycinnamate in 57% yield, m. 74-5.degree., and fluorescing strongly under ultraviolet light. The following derivs. of .alpha.-cyanocinnamate were also prepd.: Et 4-(diethylamino)-2-hydroxy, m. 147-9.degree., from 2-hydroxy-4-diethylaminobenzaldehyde, m. 62.degree., and II; cyanoethyl 4-(diethylamino)-2-ethoxy, b0.7-0.8 150-4.degree., from I and cyanoethyl cyanoacetate; Et 4-(diethylamino)-2-methoxy from 2-methoxy-4-diethylaminobenzaldehyde and II; Et 4-(diethylamino)-2-chloro, m. 83.5.degree., from 2-chloro-4-diethylaminobenzaldehyde, b0.6 132-5.degree., and II; cyanomethyl 2-chloro-4-diethylamino, m. 98-100.degree.; cyanoethyl 2-methyl-4-[bis(ethylcarboxyethyl)-**amino**], m. 122-4.degree.; cyanoethyl 4-[bis(ethylcarboxyethyl)-**amino**], m. 104-8.degree.; and Et 2-chloro-4-[bis(ethylcarboxyethyl)-**amino**], m. 64-5.degree.. The essentially H2O-insol. dyes are applied directly to fabric as aq. suspensions or dispersions.

IT **101586-75-8**, Cinnamic acid, .alpha.-cyano-4-diethylamino-2-hydroxy-, ethyl ester **101602-91-9**, Cinnamic acid, .alpha.-cyano-4-diethylamino-2-methoxy-, ethyl ester
(prepn. of)

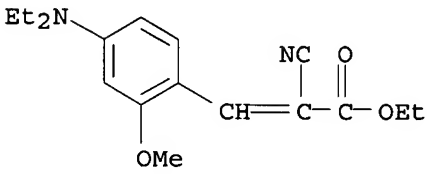
RN 101586-75-8 CAPLUS

CN Cinnamic acid, .alpha.-cyano-4-diethylamino-2-hydroxy-, ethyl ester (6CI) (CA INDEX NAME)



RN 101602-91-9 CAPLUS

CN 2-Propenoic acid, 2-cyano-3-[4-(diethylamino)-2-methoxyphenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 157 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1956:9008 CAPLUS

DOCUMENT NUMBER: 50:9008

ORIGINAL REFERENCE NO.: 50:1956h-i,1957a-b

TITLE: Competitive inhibition of 3,4-dihydroxyphenylalanine (dopa) decarboxylase in vitro

AUTHOR(S): Hartman, Wm. J.; Akawie, Richard I.; Clark, Wm. G.

CORPORATE SOURCE: Univ. of California, Los Angeles

SOURCE: Journal of Biological Chemistry (1955), 216, 507-29
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

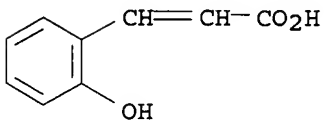
AB cf. C.A. 49, 10401f. Several previously undescribed properties of mammalian dopa decarboxylase are reported. It is completely inactivated by simultaneous addn. of substrate and 3-chloromercuribenzoic acid (final concn. 10-4M) but is not affected if it is 1st protected with glutathione. The enzyme contains an essential thiol group which is not readily attacked. The dialyzed enzyme was not reactivated either by pyridoxal-5-phosphate or by phosphate alone but 95% of the activity was regained when both were added. The inactivity of chelating agents indicates that the enzyme is not metal-dependent or that the metal is tightly bound. Erythro-3-hydroxyphenylserine, 2-methyl-3,4-

dihydroxyphenylalanine, a[redacted]6-methyl-3,4-dihydroxyphenylala[redacted]ne are substrates of dopa decarbo[redacted]lase; 46 other phenylalanine analogs were found not to be substrates. Some 200 substances were tested as inhibitors of dopa decarboxylase; the best inhibitors have the general structure 3,4-(HO)2C6H3C-:C-C(:O)X, where X is OH, **alkoxy**, alkyl, or aryl, the activity increasing in that order. The most powerful inhibitor is 5-(3,4-dihydroxycinnamoyl)salicylic acid (I), which inhibits 87% at a concn. 10-3 that of the substrate. The inhibition of dopa decarboxylase by 3-hydroxycinnamic acid (II), caffeic acid (III), and I is competitive. II and III are fairly specific inhibitors of dopa decarboxylase, since they do not appreciably affect other isolated enzyme systems. Paper chromatography showed that III decreases the amt. of dopamine formed by decarboxylation of dopa.

IT **583-17-5**, Cinnamic acid, o-hydroxy-
(derivs., dopa decarboxylase inhibition by)

RN 583-17-5 CAPLUS

CN 2-Propenoic acid, 3-(2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



L24 ANSWER 158 OF 158 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1944:39037 CAPLUS

DOCUMENT NUMBER: 38:39037

ORIGINAL REFERENCE NO.: 38:5812b-d

TITLE: Catalytic reduction of nitrocinnamic acids and esters

AUTHOR(S): Blout, Elkan R.; Silverman, Dorothy C.

SOURCE: Journal of the American Chemical Society (1944), 66, 1442-3
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

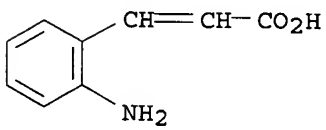
LANGUAGE: Unavailable

AB EtOH suspensions of O2NC6H4CH:CHCO2H (I) are rapidly reduced with Raney Ni under a pressure of 2-3 atm. H at 20-30.degree.; the rate of H absorption remains steady until 3 mol. equivs. have been consumed, after which the rate drops to between 0.3 and 0.01 of its former value. The acid is reduced more slowly than the Me ester. p-I in 6 hrs. gives 73% of p-H2NC6H4CH:CHCO2H (II); the Me ester of p-I in 3 hrs. gives 76% of the Me ester of II, m. 125-7.degree. (Bz deriv., m. 187.5-8.degree.). The .alpha.-Me deriv. of p-I in 6 hrs. gives 84% of .alpha.-methyl-paminocinnamic acid, m. 197-8.degree. (decompn.) (Bz deriv., m. 239-40.degree.). m-I in 12 hrs. gives 76% of m-II; the Me ester in 4.5 hrs. gives 81% of the Me ester of m-II (Bz deriv., m. 144-6.degree.). .omicron.-I in 5 hrs. gives 37% of .omicron.-II and in 16 hrs. 90% of hydrocarbostyril (III). The Me ester of .omicron.-I in 1.5 hrs. gives 74% of the Me ester of .omicron.-II (Bz deriv., m. 176-7.degree.) and in 4.5 hrs. 79% of III.

IT **1664-63-7**, Cinnamic acid, o-**amino**- **92855-96-4**, Cinnamic acid, o-benzamido-
(prepn. of)

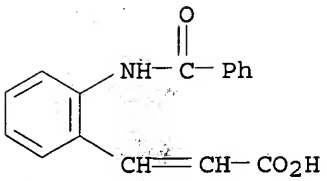
RN 1664-63-7 CAPLUS

CN 2-Propenoic acid, 3-(2-aminophenyl)- (9CI) (CA INDEX NAME)



RN 92855-96-4 CAPLUS

CN Cinnamic acid, O-benzamido- (7CI) (CA INDEX NAME)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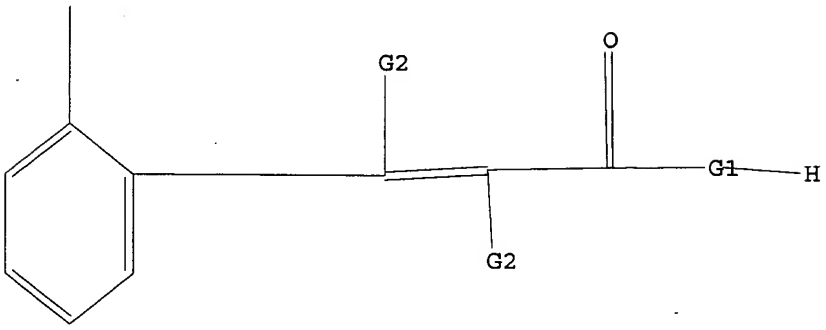

G1 O,NH,S

G2 H,Me

G3 OH,SH

Structure attributes must be viewed using STN Express query preparation.

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Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 17:03:36 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1549 TO ITERATE

64.6% PROCESSED 1000 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 28620 TO 33340
PROJECTED ANSWERS: 5084 TO 7184

L26 50 SEA SSS SAM L25

L27 7 L26

=> d 1-7 ibib abs hitstr

L27 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:454270 CAPLUS
DOCUMENT NUMBER: 139:36341
TITLE: Preparation of cinnamic acids for induction of apoptosis in cancer cells
INVENTOR(S): Dawson, Marcia I.; Fontana, Joseph A.; Zhang, Xiao-Kun; Leid, Mark; Jong, Ling; Hobbs, Peter
PATENT ASSIGNEE(S): The Burnham Institute, USA
SOURCE: PCT Int. Appl., 140 pp.

CODEN [redacted]IXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003048101	A1	20030612	WO 2002-US38506	20021202

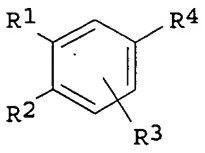
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003176506	A1	20030918	US 2002-308241	20021202

PRIORITY APPLN. INFO.: US 2001-334081P P 20011130
US 2002-406252P P 20020826

OTHER SOURCE(S): MARPAT 139:36341
GI



I

AB The present invention provides cinnamic acids (shown as I; variables defined below; e.g. (E)-4-[3-(1-Adamantyl)-4-hydroxyphenyl]-3-chlorocinnamic acid (3-Cl-AHPC)) that are inducers or inhibitors of apoptosis or apoptosis preceded by cell-cycle arrest. The present invention provides pharmaceutical compns. and methods for treating mammals with leukemia or other forms of cancer or for treating disease conditions caused by apoptosis of cells. The ability of 3-Cl-AHPC to inhibit the growth of human myeloid leukemia cells was assessed using the human acute megakaryocytic leukemia cell line M07e; exposure of these cells to varying concns. of 3-Cl-AHPC over time resulted in the progressive increase in the inhibition of proliferation; this progressive increase in growth inhibition was accompanied by the onset of apoptosis when 3-Cl-AHPC concns. of 0.5 and 1.0 .mu.M were used; while exposure to 0.2 .mu.M 3-Cl-AHPC resulted in inhibition of growth, no significant increase in apoptosis was noted. In contrast, trans-retinoic acid, a potent activator of the retinoic acid nuclear receptors, did not significantly inhibit M07e proliferation or induce apoptosis in these cells. Results of studies are reported for inhibition of leukemic cell colony formation, inhibition of CFU-GM colony formation, and induction of caspase activity by 3-Cl-AHPC; activation of mitogen-activated protein kinase pathways during 3-Cl-AHPC-mediated apoptosis; 3-Cl-AHPC induction of apoptosis of cancer cells; in vitro efficacy of 3-Cl-AHPC against breast carcinoma cells; in vitro efficacy of 3-Cl-AHPC against primary cultures of human acute myeloid leukemia cells; and 3-Cl-AHPC inhibition of in vivo growth of breast cancer. Although the methods of prepn. are not claimed, 22 example prepns. are included. For I: R1 is C1-10alkyl, C2-10alkenyl, C2-10alkynyl, halo, haloC1-10alkyl, C1-10alkoxy, (C1-10alkyl)mercapto, amino, (C1-10alkyl)NH-, (C1-10alkyl)2N-, C3-8cycloalkyl, C3-8cycloalkenyl, C6-30polycycloalkyl, C6-30polycycloalkenyl, C3-8heterocycloalkyl, C6-30polyheterocycloalkyl, C3-8heterocycloalkenyl, C3-30polyheterocycloalkenyl, aryl, heteroaryl, (C1-10alkyl)C(O)-, (C3-8cycloalkyl)C(O)-, (C3-8cycloalkenyl)C(O)-, (C3-8heterocycloalkyl)C(O)-, or (C3-8heterocycloalkenyl)C(O)-. R2 is H, hydroxy, -SH, amino, -CN, (C1-10alkyl)NH-, (C1-10alkyl)2N-, -COOR14, -C(O)R14, -C(O)N(R14)2, -N(R14)C(O)R14, -P(O)(OR14)2 (phosphonic acid), -S(O)2OR14 (sulfonic

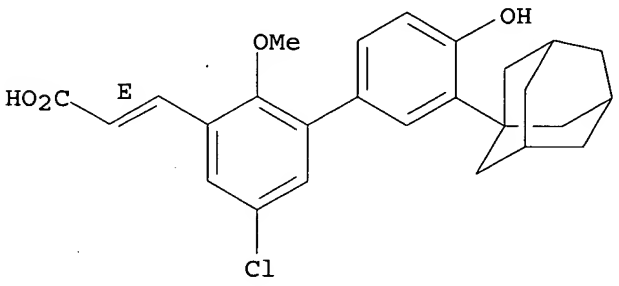
acid), -S(O)2N(R14)2 (sulfonamide), -N-C(NH)N(R15)2 (guanidino), (hydroxy)C1-10alkylene-, (C1-10alkyl)C(O)-, -C(O)NHOR14 (hydroxamic acid), or oxime. R3 is H, C1-10alkyl, hydroxy, amino, (C1-10alkyl)NH-, (C1-10alkyl)2N-, -COOR14 (carboxylic acid), -P(O)(OR14)2 (phosphonic acid), -S(O)2OR14 (sulfonic acid), -S(O)2N(R14)2 (sulfonamide), -N-C(NH)N(R15)2 (guanidino), (hydroxy)C1-10alkylene, (C1-10alkyl)C(O)-, -C(O)NHOR14 (hydroxamic acid), carbonyl oxime, fluoro, chloro, bromo, iodo, -CF3 or nitro; or R1 and R3 taken together with the ring to which they are attached can form a polycyclic group which can be fully satd., partially satd. or arom. R4 is naphthalen-2-yl, quinolin-7-yl, isoquinolin-7-yl, indol-5-yl, indol-2-yl, chroman-6-yl, quinolin-2-yl, isoquinolin-3-yl, Ph (with/without ring atom replacement by S or N), -C(O)R (R = 5-membered hetero ring radical); addnl. details are given in the claims.

IT **540778-97-0P**, (E)-5-[3-(1-Adamantyl)-4-hydroxyphenyl]-3-chloro-6-methoxycinnamic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of cinnamic acids for induction of apoptosis in cancer cells)

RN 540778-97-0 CAPLUS

CN 2-Propenoic acid, 3-(5-chloro-4'-hydroxy-2-methoxy-3'-tricyclo[3.3.1.13,7]dec-1-yl[1,1'-biphenyl]-3-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:454065 CAPLUS
DOCUMENT NUMBER: 139:53304
TITLE: Preparation of tyrosylpiperazine derivatives as P2X7 receptor antagonists
INVENTOR(S): Jacobson, Kenneth A.
PATENT ASSIGNEE(S): Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047515	A2	20030612	WO 2002-US38126	20021127

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, , ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-334130P P 20011130

OTHER SOURCE(S): MARPAT 139:53304

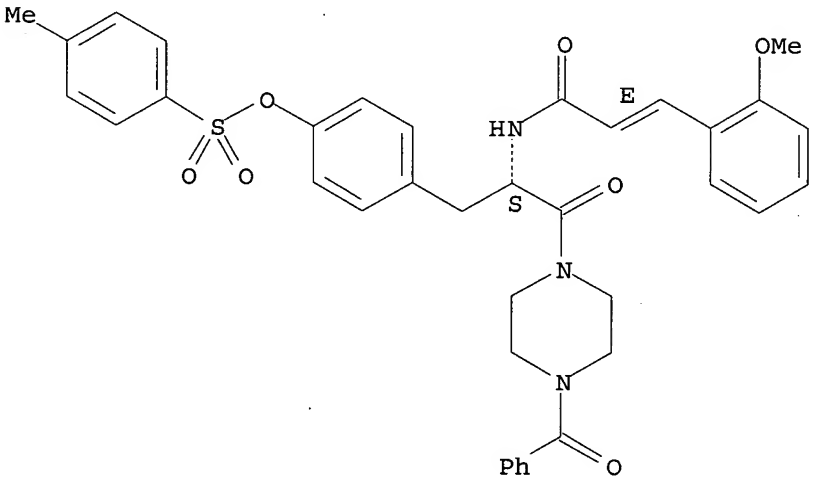
AB Disclosed are antagonists of the P2X7 receptor in an animal, e.g., tyrosylpiperazine derivs. (S)-p-R2OC6H4CH2CH(NR1R4)CO-NC4H8N-R3 [NC4H8N is piperazine; R1-R3 are sulfonyl or carbonyl groups, e.g., alkyl- or arylsulfonyl or -carbonyl; R4 is H or alkyl], which may be monomeric or dimeric. Pharmaceutical compns. comprising one or more of these antagonists are used to block an ATP-induced toxic process in the blood cell of an animal, e.g., in the treatment or prevention of septic shock, inflammation, stroke or neurodegenerative disease. Thus, [N,O-bis(quinolinesulfonyl)-L-tyrosyl]-Boc-piperazine (Boc = tert-butoxycarbonyl) was prepd. by sulfonylation of L-tyrosyl-Boc-piperazine and showed 77 .+-. 20 % inhibition of ATP-induced K+ release and IC50 .apprx. 40 nM as antagonist of P2X7 receptor-mediated ion flux.

IT **473926-25-9P**, MRS 2405
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tyrosylpiperazine derivs. as P2X7 receptor antagonists)

RN 473926-25-9 CAPLUS

CN 2-Propenamide, N-[(1S)-2-(4-benzoyl-1-piperazinyl)-1-[[4-[[(4-methylphenyl)sulfonyl]oxy]phenyl]methyl]-2-oxoethyl]-3-(2-methoxyphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L27 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:154382 CAPLUS

DOCUMENT NUMBER: 138:187795

TITLE: Preparation of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivatives as antagonists of prostaglandin E2 (PEG2) receptors

INVENTOR(S): Tani, Kousuke; Asada, Masaki; Kobayashi, Kaoru; Narita, Masami; Ogawa, Mikio

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 1009 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

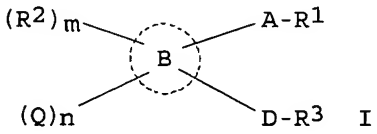
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016254	A1	20030227	WO 2002-JP8120	20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-241867 A 20010809
OTHER SOURCE(S): MARPAT 138:187795

GI



I

AB Carboxylic acid derivs. (I) and nontoxic salts thereof [wherein R1 = CO2H, CO2R4, CH2OH, COR5SO2R6, CONH2, CH2NR5SO2R6, CH2NR9COR10, CH2NR9CONR5SO2R6, CH2SO2NR9COR10, CH2O2CNR5SO2R6, tetrazole, 1,2,4-oxadiazol-5-one, 1,2,4-oxadiazol-5-thione, 1,2,4-thiadiazol-5-one, etc. (wherein R4 = C1-6 alkyl, hydroxy-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, carboxy-C1-4 alkyl, etc.; R5, R9 = H, C1-6 alkyl; R6 = C1-6 alkyl, C3-15 mono-, di-, or tricarbocyclic, 3- to 13-membered mono-, di-, or tricyclic heterocyclyl, etc.; R10 = H, R6); A = a single bond, C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, etc.; the ring B = C3-12 mono- or dicyclic carbocyclic ring, 3- to 12-membered mono- or dicyclic heterocyclic ring; R2 = C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C2-6 alkenyl, C2-6 alkynyl, halo, CHF2, CF3, NO2, cyano, Ph, oxo; m, n = 0,1,2; Q = (C1-4 alkylene, C2-4 alkenylene, or C2-4 alkynylene)-Cyc2, -C1-4 alkylene-Z-Cyc3, amino-C1-4 alkyl, cyano-C1-4 alkyl, acylamino-C1-4 alkyl, 3- to 7-membered monocyclic carbocyclyl, 3- to 6-membered monocyclic heterocyclyl, etc. (wherein Cyc2, Cyc3 = C3-15 mono-, di-, or tricyclic carbocyclyl or heterocyclyl, etc.; Z = O, S, SO, SO2, NH, NHCO, etc.); D = an linking chain consisting of 1-2 or 3-6 of atoms selected from C, N, O, or S, etc.; R3 = C1-6 alkyl, C3-15 mono-, di-, or tricyclic carbocyclyl, 3- to 15-membered mono-, di-, or tricyclic heterocyclyl, etc.] are prepd. These carboxylic acid derivs. include phenylpropanoic acid, phenylpropenoic acid, phenylpropanamide, phenylpropenamide, 3-oxoisoindolin-1-ylacetic acid, benzylbenzoic acid, benzylaminoacetic acid, pyrazolylmethylbenzoic acid, benzoylaminoacetic acid, (pyrazolylmethylphenyl)propenoic acid, pyrazolylmethylpropanoic acid, (pyridinyloxyphenyl)propanoic acid, phenoxyacetic acid, phenylbutanoic acid, (pyrazolylmethyl)propanamide, (piperazinylmethylphenyl)propanamide, (morpholinylmethylphenyl)propanamide, (pyridinyloxyphenyl)propanamide, (pyrazolylmethyl)propenamide (oxoimidazolidinylmethylphenyl)propanamide, (oxopyrrolidinylmethylphenyl)propenamide, (thiophenylmethylphenyl)propenamide, (pyrazolylmethylphenylamino)acetamide, (thiazolylaminomethylphenyl)propanamide, thiophenylpropenamide, (pyrazolylmethylphenoxy)acetamide, (phenoxymethyl)benzamide, (pyrazolylmethylphenylethyl)-1,2,4-oxadiazol-5-one, and (pyrazolylmethylphenylindolyl)acetic acid. Because of binding to PEG2 receptors, in particular, subtype EP3 and/or subtype EP4 and having antagonism, the compds. I are useful in preventing and/or treating diseases such as pain, allodynia, hyperalgesia, pruritus (itching), urticaria, atopic dermatitis, contact dermatitis, Urushi (Japanese lacquer tree) dermatitis, allergic conjunctivitis, symptoms during dialysis, asthma, rhinitis, allergic rhinitis, nasal congestion, sneeze, psoriasis, pollakiuria (increased urinary frequency), urination disorder, ejaculation (semination) disorder, fever (pyrexia), systemic inflammation reaction, learning disorder, Alzheimer's disease, neovascularization, cancer formation, cancer proliferation, cancer metastasis to organs, cancer

metastasis to bone, hyperc[redacted]emia accompanied by cancer met[redacted]asis to bone, retinopathy, rubrum, erythema (rash), leucoma, skin moth-patch, heat burn, burn, steroid burn, kidney failure, nephropathy, acute or chronic nephritis, blood electrolyte disorder, imminent abortion, threatened abortion, excessive menstruation, dysmenorrhea, endometriosis, premenstrual syndrome, uterine gland myopathy, reprodn. disorder, and stress. They are also useful in preventing and/or treating anxiety, depression, psychophysiol. disorder, mental retardation, thrombus, embolism, transient ischemic attack, cerebral infarction, atheroma, organ transplant, heart failure, hypertension, myocardial infarction, arteriosclerosis, circulation disorders or ulcers assocd. therewith, nerve disorders, vascular dementia, edema, diarrhea, constipation, biliary excretion disorder, ulcerative colitis, Crohn's disease, irritable bowel syndrome, redn. of rebound after using steroid drugs, aids for decreasing or removing steroid drugs, bone diseases, systemic granuloma, immune diseases, pyorrhea alveolaris, gingivitis, periodontal disease, nerve cell death, lung disorder, liver disorder, acute hepatitis, myocardial ischemia, Kawasaki disease, multiple organ failure, chronic headache, angiitis, venous failure, varicose vein (varicosis), anal fistula, diabetes insipidus, neonatal patent ductus arteriosus, and cholelithiasis. Thus, 4-hydroxymethyl-2-[2-(naphthalen-2-yl)ethoxy]cinnamic acid Et ester was mesylated by methanesulfonyl chloride in the presence of Et3N in THF at 0.degree. for 15 min and condensed with pyrazole in the presence of NaH in DMF at 0.degree. to give 2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid Et ester. 4-[2-[[2-(Naphthalen-1-yl)propanoyl]amino]-4-methylthiomethylphenyl]butanoic acid inhibited the binding of [3H]PGE2 to prostaglandin E2 (PEG2) receptor subtype EP1, Ep2, EP3, and EP4 expressed in CHO cells with Ki of >10, >10, 0.27, and 0.038 .mu.M, resp. A tablet formulation contg. (2E)-2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid was described.

IT **499143-50-9P**

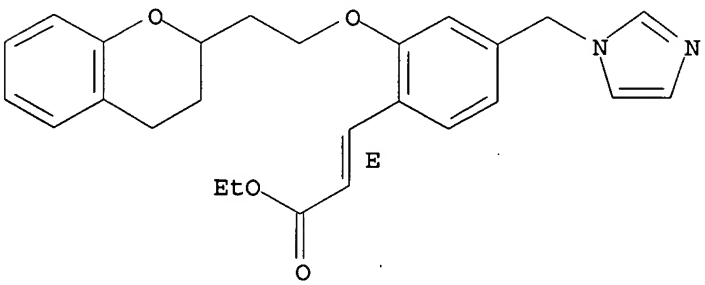
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivs. as antagonists of prostaglandin E2 (PEG2) receptors as therapeutic agents)

RN 499143-50-9 CAPLUS

CN 2-Propenoic acid, 3-[2-[2-(3,4-dihydro-2H-1-benzopyran-2-yl)ethoxy]-4-(1H-imidazol-1-ylmethyl)phenyl]-, ethyl ester, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **499143-65-6P 499143-68-9P 499144-08-0P 499151-46-1P**

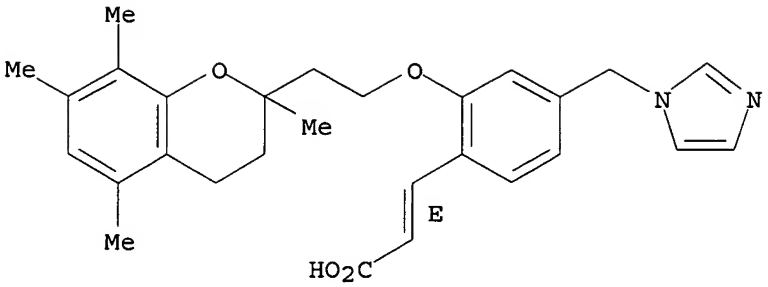
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivs. as antagonists of prostaglandin E2 (PEG2) receptors as therapeutic agents)

RN 499143-65-6 CAPLUS

CN 2-Propenoic acid, 3-[2-[2-(3,4-dihydro-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)ethoxy]-4-(1H-imidazol-1-ylmethyl)phenyl]-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

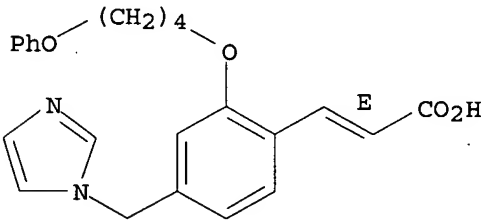
Double bond geometry as shown.



● HCl

RN 499143-68-9 CAPLUS
CN 2-Propenoic acid, 3-[4-(1H-imidazol-1-ylmethyl)-2-(4-phenoxybutoxy)phenyl]-, monohydrochloride, (2E)- (9CI) (CA INDEX NAME)

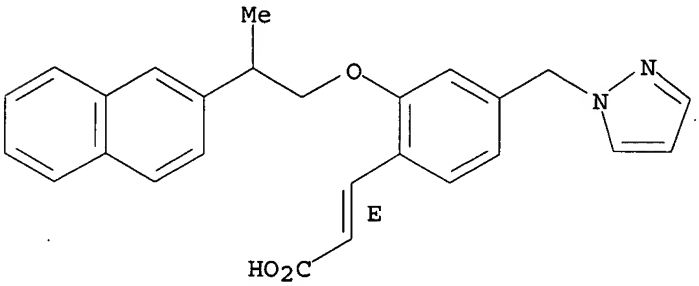
Double bond geometry as shown.



● HCl

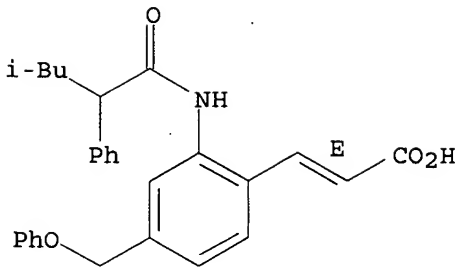
RN 499144-08-0 CAPLUS
CN 2-Propenoic acid, 3-[2-[2-(2-naphthalenyl)propoxy]-4-(1H-pyrazol-1-ylmethyl)phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

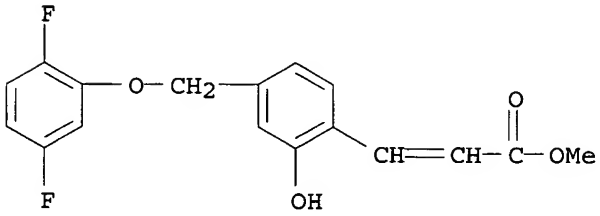


RN 499151-46-1 CAPLUS
CN 2-Propenoic acid, 3-[2-[(4-methyl-1-oxo-2-phenylpentyl)amino]-4-(phenoxymethyl)phenyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **499157-88-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivs. as antagonists of prostaglandin E2 (PEG2) receptors as therapeutic agents)
RN 499157-88-9 CAPLUS
CN 2-Propenoic acid, 3-[4-[(2,5-difluorophenoxy)methyl]-2-hydroxyphenyl]-, methyl ester (9CI) (CA INDEX NAME)



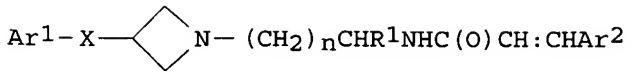
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:76603 CAPLUS
DOCUMENT NUMBER: 138:122545
TITLE: Preparation of azetidine-containing amides and their use as CCR-3 receptor antagonists
INVENTOR(S): Bhalay, Gurdip; Howe, Trevor John; Le Grand, Darren Mark; Walker, Clive Victor
PATENT ASSIGNEE(S): Novartis Ag, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft M.B.H.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007939	A1	20030130	WO 2002-EP7925	20020716

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR

PRIORITY APPLN. INFO.: GB 2001-17387 A 20010717
OTHER SOURCE(S): MARPAT 138:122545
GI



I

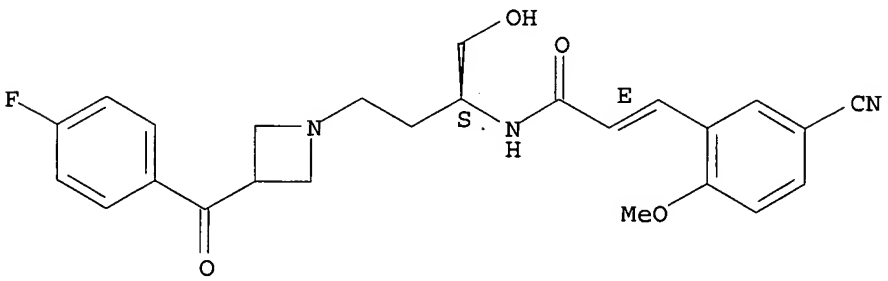
AB The invention relates to azetidine derivs. (I; variables defined below; e.g. (E)-N-[(S)-1-tert-butoxymethyl-3-[3-(4-fluorophenoxy)azetidin-1-yl]propyl]-3-(5-cyano-2-methoxyphenyl)acrylamide) in free or salt form. Compns. contg. them, methods for their prepn. and their use as pharmaceuticals are also described. The agents of the invention act as CCR-3 receptor antagonists, thereby inhibiting the infiltration and activation of inflammatory cells, particularly eosinophils, and inhibiting allergic response. The effect of agents of the invention on the binding of human eotaxin to human CCR-3 was detd. Eighteen I have IC50 values <1 .mu.M in the above assay. For instance, (E)-N-[(S)-1-tert-butoxymethyl-3-[3-(4-fluorophenoxy)azetidin-1-yl]propyl]-3-(5-cyano-2-methoxyphenyl)acrylamide has an IC50 value of 1 nM. Most of the 18 I exhibit selectivity for inhibition of CCR-3 binding relative to inhibition of binding of the alpha-1 adrenergic receptor. Eighteen example prepns. of I are included. For example, the above I was prepd. via intermediates [(S)-1-tert-butoxymethyl-3-iodopropyl]carbamic acid benzyl ester, [(S)-1-tert-butoxymethyl-3-[3-(4-fluorophenoxy)azetidin-1-yl]propyl]carbamic acid benzyl ester, and (S)-1-tert-butoxymethyl-3-[3-(4-fluorophenoxy)azetidin-1-yl]propylamine. For I: Ar1 is Ph substituted by .gtoreq.1 halogen atoms; Ar2 is Ph optionally substituted by .gtoreq.1 halogen, cyano, hydroxy, nitro, C1-C8-alkyl, C1-C8-haloalkyl, C1-C8-alkoxy, C1-C8-alkoxycarbonyl or di(C1-C8-alkyl)aminocarbonylmethoxy; R1 is H or C1-C8-alkyl optionally substituted by hydroxy, C1-C8-alkoxy, acyloxy, halogen, carboxy, C1-C8-alkoxycarbonyl, -N(R2)R3, -CON(R4)R5 or by a monovalent cyclic org. group having 3-15 atoms in the ring system. R2 and R3 are each independently H or C1-C8-alkyl, or R2 is H and R3 is hydroxy-C1-C8-alkyl, acyl, -SO2R6 or -CON(R4)R5, or R2 and R3 together with the N atom to which they are attached denote a 5- or 6-membered heterocyclic group; R4 and R5 are each independently H or C1-C8-alkyl, or R4 and R5 together with the N atom to which they are attached denote a 5- or 6-membered heterocyclic group; R6 is C1-C8-alkyl, C1-C8-haloalkyl, or Ph optionally substituted by C1-C8-alkyl; X is -C(O)-, -O- or -CH2-; and n is 1, 2, 3 or 4.

IT **490021-88-0P**, (E)-3-(5-Cyano-2-methoxyphenyl)-N-[(S)-3-[3-(4-fluorobenzoyl)azetidin-1-yl]-1-hydroxymethylpropyl]acrylamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of azetidine-contg. amides and their use as CCR-3 receptor antagonists)

RN 490021-88-0 CAPLUS

CN 2-Propenamide, 3-(5-cyano-2-methoxyphenyl)-N-[(1S)-3-[3-(4-fluorobenzoyl)-1-azetidinyl]-1-(hydroxymethyl)propyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



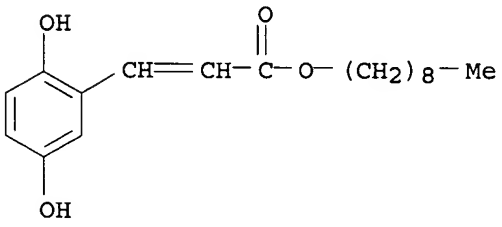
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2002:[redacted]366 CAPLUS
DOCUMENT NUMBER: 138:385123
TITLE: Synthesis and antitumor activity of alkyl 2,5-dihydroxycinnamates
AUTHOR(S): Nguyen, Hai Nam; Ahn, Byung-Zun
CORPORATE SOURCE: College of Pharmacy, Chungnam National University, S. Korea
SOURCE: Tap Chi Hoa Hoc (2002), 40(3), 111-115
CODEN: TCHHDC; ISSN: 0378-2336
PUBLISHER: Toa Soan Tap Chi Hoa Hoc
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:385123

AB A series of alkyl 2,5-dihydroxycinnamates (2a.apprx.i) were synthesized and evaluated for cytotoxicity and antitumor activity. The cytotoxicity decreased with alkyl chains from Me to n-pentyl. However, further prolongation proved to be beneficial for bioactivity with cytotoxicity peaked when alkyl chain being n-nonyl (2i). Two compds. 2a and 2i showed significant antitumor activities in BDF1/B16 model.

IT **528603-13-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of alkyl 2,5-dihydroxycinnamates and antitumor activity thereof)

RN 528603-13-6 CAPLUS
CN 2-Propenoic acid, 3-(2,5-dihydroxyphenyl)-, nonyl ester (9CI) (CA INDEX NAME)



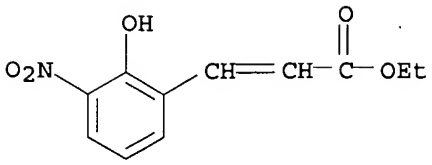
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:835620 CAPLUS
DOCUMENT NUMBER: 139:22119
TITLE: Product class 13: benzoxazoles and other annulated oxazoles
AUTHOR(S): Boyd, G. V.
CORPORATE SOURCE: Givataim, 53460, Israel
SOURCE: Science of Synthesis (2002), 11, 481-492
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review describes the different methods for the synthesis of benzoxazoles and other annulated oxazoles.

IT **538311-22-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of benzoxazoles and annulated oxazoles via ring closing reactions or ring transformation reactions)

RN 538311-22-7 CAPLUS
CN 2-Propenoic acid, 3-(2-hydroxy-3-nitrophenyl)-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

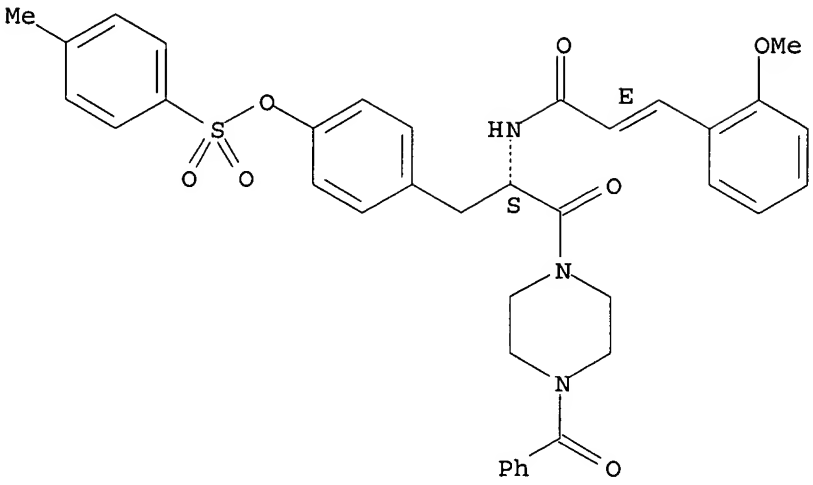
L27 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:655505 CAPLUS
DOCUMENT NUMBER: 137:338109
TITLE: Functionalized Congeners of Tyrosine-Based P2X7 Receptor Antagonists: Probing Multiple Sites for Linking and Dimerization
AUTHOR(S): Chen, Wangzhong; Ravi, R. Gnana; Kertesy, Sylvia B.; Dubyak, George R.; Jacobson, Kenneth A.
CORPORATE SOURCE: Molecular Recognition Section, Laboratory of Bioorganic Chemistry, National Institute of Diabetes Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA
SOURCE: Bioconjugate Chemistry (2002), 13(5), 1100-1111
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Chem. functionalized analogs of antagonists of the P2X7 receptor, an ATP-gated cation channel, were synthesized as tools for biophys. studies of the receptor. These functionalized congeners were intended for use in chem. conjugation with retention of biol. potency. The antagonists were L-tyrosine derivs., related to [N-benzyloxycarbonyl-O-(4-arylsulfonyl)-L-tyrosyl]benzoylpiperazine [such as MRS2409 (I)]. The analogs were demonstrated to be antagonists in an assay of human P2X7 receptor function, consisting of inhibition of ATP-induced K+ efflux in HEK293 cells expressing the recombinant receptor. The analogs were of the general structure R1-Tyr(OR2)-piperazinyl-R3, in which three positions (R1-R3) were systematically varied in structure through introduction of chem. reactive groups. Each of the three positions was designed to incorporate a 3- or 4-nitrophenyl group. The nitro groups were reduced using NaBH4-copper(II) acetylacetonate to amines, which were either converted to the isothiocyanate groups, as potential affinity labels for the receptor, or acylated, as models for conjugation. An alternate route to N.alpha.-3-aminobenzyloxycarbonyl functionalization was devised. The various positions of functionalization were compared for effects on biol. potency, and the R2 and R3 positions were found to be most amenable to derivatization with retention of high potency. Four dimeric permutations of the antagonists were synthesized by coupling each of the isothiocyanate derivs. to either the precursor amine or to other amine congeners. Only dimers linked at the R2-position were potent antagonists. In concn.-response studies, two derivs., a 3-nitrobenzyloxycarbonyl deriv. (II) and a 4-nitrotoluenesulfonate (III), displayed IC50 values of roughly 100 nM as antagonists of P2X7 receptor-mediated K+ flux.

IT **473926-25-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and P2X7 receptor antagonist activity of)
RN 473926-25-9 CAPLUS
CN 2-Propenamide, N-[(1S)-2-(4-benzoyl-1-piperazinyl)-1-[[4-[[(4-methylphenyl)sulfonyl]oxy]phenyl]methyl]-2-oxoethyl]-3-(2-methoxyphenyl)-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	32.17	740.98

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.56	-16.94

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